Attorney Docket No. 9233. DV2

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In the claims:

Please amend the claims as follows:

1-45. (canceled)

- 46. (currently amended) A method for inducing analgesia in a subject in need thereof, comprising <u>delivering across the blood brain barrier of the subject</u> administering to the subject a therapeutically effective amount of an amphiphilic drug-oligomer conjugate comprising an opioid conjugated to an oligomer, wherein the oligomer comprises one or more lipophilic moieties coupled to one or more hydrophilic moieties.
- 47. (previously presented) The method of Claim 46 wherein the opioid is enkephalin (SEQ ID NO:48).
- 48. (previously presented) The method of claim 46 wherein the one or more lipophilic moiety is selected from the group consisting of fatty acids, C_{1-26} alkyls, and cholesterol.
- 49. (previously presented) The method of claim 46 wherein the one or more hydrophilic moieties are selected from the group consisting of sugars and PEG.
- 50. (withdrawn) The method of claim 46 wherein the one or more hydrophilic moieties comprise a sugar selected from the group consisting of amino sugars and non-amino sugars.

51-60. (canceled)

61. (withdrawn) The method of claim 48 wherein the oligomer is consisting of:

 $CH_3(CH_2)_n(OC_2H_4)_mOH$

(Formula 1),



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wherein n=3 to 25 and m1 to 6;

 $CH_3(CH_2)_n(OC_2H_4)_mOCH_2CO_2H$

(Formula 2),

wherein n=3 to 25 and m=1 to 7;

 $CH_3(CH_2)_nCX(OC_2H_4)_mOH$

(Formula 3),

wherein n=3 to 25, m=1 to 7 and X=O or N;

 $R-(OC_2H_4)_mCH_2CO_2H$

(Formula 4),

wherein m=0 to 5 and R=cholesterol or adamantane; or

 $R-OCO(C_2H_4O)_mCH_2CO_2H$

(Formula 5),

wherein m=0 to 5;

 $CH_3(CH_2-CH=CH)_6(CH_2)_2C_{H2}(OC_2H_4)_mOH$

(Formula 6),

wherein m=0 to 7;

 $CH_3(CH_2-CH=CH)_6(CH_2)_2C_x(OC_2H_4)_mOH$

(Formula 7),

wherein m=1 to 7 and X=N or O.

62. (withdrawn) The amphiphilic drug-oligomer conjugate of claim 1 wherein the therapeutic compound is a peptide and the peptide is selected from the group consisting of:

 $\label{eq:conditional_condition} Ac-Phe-Arg-Trp-Trp-Tyr-Lys-NH_2;$

Ac-Arg-Trp-lle-Gly-Trp-Lys-NH₂;

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Trp-Trp-Pro-Lys-His-Xaa—NH2,

wherein Xaa is a naturally-occurring amino acid;

Trp-Trp-Pro-Xaa—NH2,

wherein Xaa is Lys or Arg;

Tyr-Pro-Phe-Gly-Phe-Xaa—NH₂;

wherein Xaa is a naturally-occurring amino acid;

(D)lle-(D)Met-(D)Ser-(D)Trp-(D)Trp-Gly_n-Xaa—NH₂, wherein n is 0 or 1 and wherein Xaa is Gly or the D-form-of a naturally-occurring amino acid;

(D)lle-(D)Met-(D)Trp-Gly-Xaa—NH2, wherein Xaa is Gly or the D-form of a naturally-occurring amino acid;

Tyr-A1-B2-C3-NH2,

wherein A1 is (D)Nve or (D)Nle,

B2 is Gly, Phe, or Trp, and

C3 is Trp or Nap;

Pm and red $\{Me_xH_y-Tyr-(NMe)_z-Tyr-Xaa_z-NH_2\}$,

x is 0, 1, or 2,

y is 0, 1, or 2, and .

z is 0 or 1, and

wherein Xaa is Phe, (D)Phe, or NHBzl, with the proviso that x and y together is never greater than 2;

Trp-Trp-Pro-D4-His_z-Xaa_z—NH2;

wherein z is 0 or 1,

wherein D4 is Lys or Arg, and

wherein Xaa is a naturally-occurring amino acid.

63. (withdrawn) The method of claim 18 wherein the therapeutic compound is a peptide and the peptide is selected from the group consisting of:

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Ac-Phe-Arg-Trp-Trp-Tyr-Lys—NH₂;

Ac-Arg-Trp-lle-Gly-Trp-Lys-NH₂;

Trp-Trp-Pro-Lys-His-Xaa—NH2,

wherein Xaa is a naturally-occurring amino acid;

Trp-Trp-Pro-Xaa—NH2,

wherein Xaa is Lys or Arg;

Tyr-Pro-Phe-Gly-Phe-Xaa-NH₂;

wherein Xaa is a naturally-occurring amino acid;

(D)lle-(D)Met-(D)Ser-(D)Trp-(D)Trp-Gly_n-Xaa—NH₂, wherein n is 0 or 1 and wherein Xaa is Gly or the D-form-of a naturally-occurring amino acid;

(D)lle-(D)Met-(D)Thr-(D)Trp-Gly-Xaa—NH2,

wherein Xaa is Gly or the D-form of a naturally-occurring amino acid;

Tyr-A1-B2-C3—NH2,

wherein A1 is (D)Nve or (D)Nle,

B2 is Gly, Phe, or Trp, and

C3 is Trp or Nap;

Pm and red $\{Me_xH_v-Tyr-(NMe)_z-Tyr-Xaa_z-NH_2\}$,

x is 0, 1, or 2,

y is 0, 1, or2, and

z is 0 or 1, and

wherein Xaa is Phe, (D)Phe, or NHBzl, with the proviso that x and y together is never greater than 2;

Trp-Trp-Pro-D4-His_z-Xaa_z—NH2;

wherein z is 0 or 1,

wherein D4 is Lys or Arg, and

wherein Xaa is a naturally-occurring amino acid.

64-69. (canceled)

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70. (previously presented) The method of claim 46 wherein the opioid is an enkephalin.

71. (previously presented) The method of claim 46 wherein the opioid is a non-naturally occurring opioid.

72. (canceled)

73. (previously presented) The method of claim 46 wherein the subject is a human.

74. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject orally.

- 75. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject intravenously.
- 76. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject by a route selected from the group consisting of pulmonary, intraosseal, intradermal, intramuscular, intraperitoneal, subcutaneous, intranasal and epidural.
- 77. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject by a route selected from the group consisting of intraventricular and intrathecal.
- 78. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject as a component of a pharmaceutical composition.

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79. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject as a component of a pharmaceutical composition formulated for oral administration.

- 80. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject as a component of a pharmaceutical composition formulated for intravenous administration.
- 81. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject as a component of a pharmaceutical composition formulated for administration by a route selected from the group consisting of pulmonary, intraosseal, intradermal, intramuscular, intraperitoneal, subcutaneous, intranasal and epidural.
- 82. (currently amended) The method of claim 46 wherein the amphiphilic drugoligomer conjugate is administered to the subject as a component of a pharmaceutical composition formulated for administration by a route selected from the group consisting of intraventricular and intrathecal.
- 83. (currently amended) A method for inducing analgesia comprising administering to a subject in need thereof comprising delivering across the blood brain barrier of the subject an analgesia-inducing amount of a cetyl-PEG₂-enkephalin (SEQ ID NO:1) conjugate.
- 84. (withdrawn) A method for inducing analgesia comprising administering to a subject in need thereof an analgesia-inducing amount of a DHA-PEG₂-enkephalin **SEQ ID NO:1)** conjugate.
- 85. (previously presented) The method of claim 46 wherein the oligomer has a formula:



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 $CH_3(CH_2)_n(OC_2H_4)_mOH$

(Formula 1),

wherein n=3 to 25 and m=1 to 6.

86. (withdrawn) The method of claim 46 wherein the oligomer has a formula:

 $CH_3(CH_2)_n(OC_2H_4)_mOCH_2CO_2H$

(Formula 2),

wherein n=3 to 25 and m=1 to 7.

87. (withdrawn) The method of claim 46 wherein the oligomer has a formula:

 $CH_3(CH_2)_nCX(OC_2H_4)_mOH$

(Formula 3),

wherein n=3 to 25, m1 to 7 and X=O or N.

88. (withdrawn) The method of claim 46 wherein the oligomer has a formula:

 $R-(OC_2H_4)_mCH_2CO_2H$

(Formula 4),

wherein m=0 to 5 and R=cholesterol or adamantane.

89. (withdrawn) The method of claim 46 wherein the oligomer has a formula:

 $R-OCO(C_2H_4O)_mCH_2CO_2H$

(Formula 5),

wherein m=0 to 4 and R=cholesterol or adamantane.

90. (withdrawn) The method of claim 46 wherein the oligomer has a formula:

 $CH_3(CH_2-CH_7 CH)_6(CH_2)_2CH_2(OC_2H_4)_mOH$

(Formula 6),

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wherein m=0 to 7.

91. (withdrawn) The method of claim 46 wherein the oligomer has a formula:

$$CH_3(CH_2-CH_7 CH)_6(CH_2)_2C_x(OC_2H_4)_mOH$$
 (Formula 7),

wherein m=1 to 7 and X=N or O.

92. (withdrawn) The method of claim 46 wherein the drug-oligomer conjugate has a formula:

93. (withdrawn) The method of claim 46 wherein the drug-oligomer conjugate has a formula:

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94. (previously presented) The method of claim 46 wherein the drug-oligomer conjugate has a formula:

O
$$\parallel$$
 H₂N-Tyr-Gly-Gly-Phe-Met-Lys-C-OH \parallel N-C-OC₂H₄OC₂H₄-O-(CH₂)₁₅-CH₃ (SEQ ID NO:1) H \parallel O

(withdrawn) The method of claim 46 wherein the drug-oligomer conjugate has a formula:

96. (withdrawn) The method of claim 46 wherein the drug-oligomer conjugate has a formula:

(SEQ ID NO:1)

$$H_2$$
N-Tyr-Gly-Gly-Phe-Met-Lys-C-OH

N-C-O(C_2H_4O)₃-C-(CH_2)₁₄- CH_3 (SEQ ID NO:1)

H

O

O

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97. (withdrawn) The method of claim 46 wherein the drug-oligomer conjugate has a formula: